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PRELIMINARY REPORT

IMMUNE RESPONSE OF GUINEA PIGS TO VARICELLA VACCINE STRAIN (OKA) AND WILD STRAINS

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An immune response (neutralizing and complement fixing antibodies) was detected in guinea pigs to varicella vaccine strain (Oka), but not to 2 wild strains. The possible use of guinea pigs and the vaccine strain (Oka) as a model system is discussed.

The sporadic occurrence of zoster has led to the idea that this disease represents reactivation of a latent infection from chickenpox. The mechanism by which the reactivation occurs is unknown, but an animal model might help in studies on how virus that is usually in a latent state escapes from the host's control. There have been few reports of successful infection of experimental animals with varicella-zoster virus (VZV). Rivers (1926, 1927) reported that he inoculated the testes of velvet and green monkeys with emulsified vesicles and papules collected from a human chickenpox rash and found intranuclear inclusion bodies in cells in regions of the testes damaged by the inoculation. This paper reports that guinea pigs are susceptibile to a varicella virus strain and might be useful as an experimental model of VZV infection.

The Oka (attenuated vaccine strain), Kawaguchi and Eguchi strains of VZV, which were isolated in our laboratory, were used in this work. Cell-free virus stocks were prepared as described elsewhere (Takahashi et al., 1975) using human embryonic lung (HEL) cells. Male white Hartley guinea pigs, weighing about 200 g, were inoculated with virus subcutaneously. Just before and one month after inoculation, blood for assay of serum neutralizing (NT) and complement fixation (CF) antibody titers was withdrawn by cardiac puncture. Serum was inactivated by heating at 56°C for 30 min before tests. NT tests were done as follows. Stock virus solution (0.1 ml containing 100 to 150 PFU of Kawaguchi strain) was mixed with 0.1 ml of serially diluted serum and 0.1 ml of fresh guinea pig serum as a source of complement, and the mixtures were incubated at 37°C for 30 min. Then 0.1 ml of these mitures was inoculated onto human embryonic fibroblast (HEF) cells in 6-well plastic plates, and incubated at

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37°C for 1 hr to allow adsorption. Then maintenance medium (Eagle MEM supplemented with 3% fetal calf serum) was added to the cultures and incubation at 37°C was continued. Cells were fixed with 5% formalin solution 5 days after infection, and stained with 0.5% methylene blue. Plaques were counted under a dissecting microscope at 20-fold magnification. Antibody titers are expressed as reciprocals of the highest dilution of serum producing 50% or more reduction in plaques. The CF antibody titer was measured as described elsewhere (Yamada et al., 1979).

Guinea pigs were injected subcutaneously with 0.5 ml of virus solution. None of the guinea pigs had any detectable NT antibody titer before injection. Six of 9 guinea pigs (66.7%) injected with Oka strain at a dose of 2.0×10^3 PFU showed an NT antibody response and 3 of 4 (75%) injected with a dose of 8.0×10^3 showed a higher antibody response. On the contrary, no guinea pigs showed any antibody response to the Kawaguchi or Eguchi strain injected at a higher dose than that of the Oka strain (Table 1).

These results suggest that of the 3 strains, only the Oka strain induced infection in guinea pigs. The Oka strain was isolated in HEL cells, passaged 11 times in HEL cells and 12 times in guinea pig embryo cells, and then propagated in human diploid cells as a vaccine. On the other hand, the other two strains were isolated from patients with varicella and passaged only in HEL cells. It is uncertain whether the passage history of the Oka strain is correlated with its immunogenicity in guinea pigs, and this requires further studies. However, the present results indicate that the Oka strain of VZV and guinea pigs might be a useful model system and also that immunogenicity in guinea pigs might be a specific marker of the vaccine strain. The latter possibility is now being examined by extensive studies on other strains.

TABLE 1. *Antibody Response in guinea pigs inoculated with various strains of VZV*

Expt. 1.

Strain	Virus titer PFU/dose	Antibody Response (4 weeks)		Seroconv. rate	
		NT Ab titer	CF Ab titer	NT	CF
Oka (Vaccine)	2.0×10^3	<4, 4, 8, 16	<4, 4, 8, 16	3/4 (75%)	3/4 (75%)
Kawaguchi (HEL 16th)	1.5×10^4	<4, <4	<4, <4	0/2 (0%)	0/2 (0%)

Expt. 2.

Strain	Virus titer PFU/dose	Antibody Response (4 weeks)	Seroconv. rate
		NT Ab titer	
Oka (vaccine)	2.0×10^3	<4, <4, 4, 8, 16	3/5 (60%)
	8.0×10^3	<4, 8, 8, 16	3/4 (75%)
Kawaguchi (HEL 16th)	1.5×10^4	<4, <4, <4, <4, <4	0/5 (0%)
Eguchi (HEL 3rd)	3.0×10^4	<4, <4, <4, <4, <4	0/5 (0%)

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